Remarks/Arguments

In response to the Rejection mailed July 27, 2004, Applicants have amended claims 82, 84, and 86, and present the following remarks.

Claims 86 and 87 were rejected under 35 USC 112, second paragraph as being indefinite. Specifically the language reciting that some of the fibers contain the same agent of interest appears to conflict with the recitation of different agents of interest being immobilized on the fibers. This rejection is respectfully traversed.

The two recitations do not conflict. One recitation indicates that one agent is immobilized on one fiber and a different agent is immobilized on a second fiber. The other recitation indicates that two fibers are present which differ by having differing concentrations of agent of interest immobilized thereon. Since the fiber bundle has many fibers both situations may be present.

A very simplified example of such a fiber bundle that fits the description of both recitations in claim 86 may contain three different fibers. Fiber 1 has agent A immobilized therein. Fiber 2 has 1 mg of agent B immobilized on 10 cm length of fiber. Fiber 3 has 10 mg of agent B immobilized on 10 cm length of fiber. Such a bundle of three fibers fills the recitation of "different agents of interest" (A being different from B) and "different concentrations of the same agent of interest (1mg of B/length being a different concentration from 10 mg of B/length).

To clarify any possible misinterpretation, clarifying amendments to claim 86 were made above.

Claims 82, 83, 86 and 87 were rejected under 35 USC 102(e) as being anticipated by Stimpson. Stimpson is cited as disclosing dipping a rod into a unique binding agent and then bundling the rods, slicing them and mounting a slice. This rejection is respectfully traversed.

The rejection indicates that small phrases in these claims were apparently missed. Claim 82 recites, "cutting the fiber bundle at an angle other than transversely to form a

section". All of the bundle cutting in Stimpson was performed transversely to the bundle. In at least four locations in their specification and claims, Stimpson emphasized cutting at right angles to the length of the bundle, for example:

"After reagent application, the membrane is rolled around a rod shaped support to form a tight spiral of membrane material similar to a "jelly roll". The outer surface is bound with a material that supplies radial compression (e.g. heat shrink insulation or adhesive tape) and the resulting roll is **cut into individual arrays along the Z-axis**. In this case, the arrays are spiral in nature with each array element formed by the freshly cut edge of the sheet material impregnated with the various binding agents."

"The spiral is bound and then cut along the z axis (i.e. the membrane sheet width) to create individual arrays with identical zones of immobilized bindings agents."

"The series of bands are revealed by cutting a rod and examination in a microscope to give the spatial distribution of the elements in all arrays in the bundle**. Note that individual rods must preserve their spatial arrangement throughout the Z-length of the bundle**."

"Example 3 ... The spiral bundle was placed inside a metal tube whose inner diameter was slightly larger than the outer diameter of the bundle. **The a 1-2 mm length of the bundle was allowed to extend from the end of the metal tube and an array slab was cut with a razor blade using the metal tube as a guide to obtain a uniform straight cut."**

Cutting at a non-transverse angle produces a different microarray that has certain advantages. For example, when a microarray produced by transverse bundle slicing with immobilized binding partners on the inside of hollow fibers is used and viewed from above, one can visualize a thin ring of labeled material. However, if one cuts the hollow fiber bundle on a non-transverse angle (such as at 45 degrees), one visualizes the inner side of each hollow fiber when the section is mounted and visualized from above. This gives a more easily detectable signal. It is also easier to shine a different wavelength of light onto the same surface to perform a fluorescence assay. Not only is Simpson silent regarding this method step, such an advantage is not suggested by Stimpson.

Regarding claims 86 and 87, entirely different recited features are not taught. These claims recite fibers with ***"different concentrations of the same agent on different fibers"***. As mentioned above regarding the rejection under 35 USC 112, these claims require the presence of at least two fibers, both with the same immobilized binding partner and one fiber having a different concentration of the agent from the other fiber. Not only does

Stimpson lack any teaching of this feature, but also such would not be suggested by the Stimpson teachings.

Stimpson immobilized their molecules on their rods or threads by immersing the rod or thread in a solution. In order to get different concentrations on different rods, Stimpson would need to make at least two different solutions, each with a different concentration of the same compound or somehow treat the rods differently before or during the immobilizing process. This is not taught. The Stimpson method of ink jet printing of a solution onto a rod (or gel strip) also does not readily lend itself to immobilizing using different concentrations or different amounts of binding partner on different rods or gel strips.

Still further, Stimpson does not recognize using a microarray with different fibers as a way for quantitatively determining the amount of analyte in a sample. The little discussion of measuring anything quantitative in Stimpson refers to conventional analysis of measuring different amounts of signal. There is no hint of measuring different signals from different fibers because the different fibers have different concentration of agent of interest. Accordingly, this rejection should be withdrawn.

Claims 16, 18, 22-24 and 81 were rejected under 35 USC 103 as being unpatentable over Stimpson. In addition to that mentioned above, the examiner contends that it would be obvious to slice sections of the claimed thickness as routine optimization or workable ranges. This rejection is respectfully traversed.

The claimed thickness is outside the taught operable ranges in Stimpson. Stimpson teaches cutting the sections very thin from as little as 0.2 mm to 1 mm thick (200 to 1,000 microns thick) as stated below in the passages from Stimpson.

"Cutting by hand can easily give arrays 1 mm in thickness so that a 8 inch (20 cm) wide sheet yields 200 arrays for each bundle. More sophisticated methods of cutting (e.g. laser light) could yield arrays of 0.2 mm in thickness and increase this number to 1000."

"Cutting the rod or spiral bundles to form the arrays can be accomplished using mechanical or laser methods. Razors or knife blades can be used to manually cut porous polymeric materials to give arrays 0.2-1 mm thick."

"Example 1 ... "The resulting bundle was cut into slabs about 1 mm in thickness to form arrays. Each array contains a section from all the rod elements."

"Example 3 ... Arrays as thin as 0.2 mm were cut by hand, albeit, not uniformly."
From these passages, it is clear that Stimpson considered these the minimum practical thickness. Therefore, the claimed thickness, which is far outside the ranges taught, is not suggested by the reference.

Furthermore, in Example 3, the arrays "as thin as 0.2 mm" represents a minimum measurement. Because this thin of a cut was "albeit, not uniformly", it is not a very practical thickness and clearly teaches away from using a thinner cut. Stimpson teaches that technical reasons provide a minimum practical thickness. Therefore, it is not reasonable for one to routinely experiment with a thickness far less than the minimum that gives even poor results.

Thirdly, applicants have demonstrated unexpected superior results using such thin sections. Applicants have found that thinner sections are actually superior to thicker sections because of less background and more than adequate agent of interest being present. Note the present specification, Example 2, where the sections were 5-20 microns thick, Example 4, where the sections were 5-100 microns thick and Example 14 where the sections were 10 microns thick. It should be particularly noted that the 10 micron thick sections gave superior results by having less background fluorescence than 50 micron thick sections.

Contrary to Stimpson where technical aspects of cutting provided an optimal range, in the present invention, the thickness used is determined by the amount of signal and background. Applicants have optimized section thickness based on different criteria and therefore the ranges are quite different and not suggested by Stimpson. Accordingly, one of ordinary skill performing routine optimization would be working toward a much thicker section based on the optimal criteria given by Stimpson. This is quite different from and results in a different thickness from the presently claimed invention. Accordingly, the rejection should be withdrawn.

Claims 84 and 85 were rejected under 35 USC 103 as being unpatentable over Stimpson in view of Walt et al. Simpson was cited to show the basic technique for immobilizing molecular binding agents onto a rod in a bundle followed by slicing the bundle

to form a microarray section. While admitting that Stimpson lacks any teaching of using biological cells or microorganism as the binding agent, the Examiner relies on Walt et al for this purpose and urges it obvious. This rejection is respectfully traversed.

Walt et al does not "have different biological cells or microorganisms immobilized in or on a length of different fibers". Walt et al have cells or microorganisms free in liquid in wells at the end of optical fibers. There is no "immobilization" along the length of the fiber. Immobilization substantially throughout a length of each fiber is important to the present invention because the claims recite cutting the bundle multiple times to make multiple sections, each with cells or microorganisms immobilized therein or thereon.

Walt et al has a well filled with a liquid suspension of biological cells or microorganisms. Even if one considers a liquid filled well as "immobilizing" its liquid contents, this still does not meet the claimed requirements. One cannot cut such a bundle multiple times and have the same biological cells or microorganisms immobilized in more than one section. Also, cutting the optical fibers of Walt et al renders the Walt et al invention inoperable and thus would not be obvious.

Furthermore, Stimpson only immobilizes compounds. There is no suggestion that living cells can be used in the Stimpson method. Stimpson uses immobilization techniques that are overly harsh and impractical for immobilizing living organisms without killing or radically changing their characteristics. Walt et al involves a different technique without immobilization along the length of the fiber. Therefore, there is no suggestion in either reference to prepare the presently claimed invention.

Claims 16-18, 81-82 and 84 were rejected under the doctrine of obviousness-type double patenting over claims 1-17 of U.S. Patent 6,713,309. Applicants request this rejection be delayed until these claims have been indicated otherwise patentable. A terminal disclaimer may be filed at that time as needed depending on the claim language otherwise allowable.

In view of the amendments and comments above, the rejections other than obviousness-type double patenting have been overcome. Reconsideration, withdrawal of the

rejections and early indication of allowable claims are respectfully requested. If any issues remain, the examiner is encouraged to telephone the undersigned.

If needed, applicants petition for an extension of time under the provisions of 37 CFR 1.136(a) for sufficient time to accept this response. The commissioner hereby is authorized to charge payment of any fees under 37 CFR § 1.17, which may become due in connection with the instant application or credit any overpayment to Deposit Account No.500933.

Respectfully submitted,

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